REMARKS:

Reconsideration of the present application is respectfully requested for the reasons that follow.

Restriction Requirement

Claims 1-21 and 24-30 were originally pending in the application. As a result of the Restriction Requirement, claims 2, 10-21 and 24-30 are withdrawn from consideration. Applicants note that the Examiner has made the Restriction Requirement final, but do not concede to the Examiner's position. Applicants expressly reserve the right to pursue the prosecution of the withdrawn subject matter in one or more divisional applications and may request rejoinder of the non-elected subject matter at a later date.

Information Disclosure Statements

The Examiner has objected to the Information Disclosure Statement (IDS) submitted on June 6, 2005 because Applicant has not submitted copies of these references. Applicants note that these references were cited in the International Search Report and should have been forwarded to the USPTO by the International Bureau. Applicants request that the Examiner consider the copies of the references forwarded by the International Bureau. If these references are not available, Applicant will provide copies.

The Examiner has objected to the IDS filed September 2, 2005 because it does not include a concise explanation of relevance of each patent listed that is not in English. In addition, the German patent document 198 19 889 does not have an English

language abstract. The Applicants note that the September 2, 2005 IDS did include a concise explanation of DE 198 19 889. In addition, Applicants have attached to this response an English translation of the DE 198 19 889 abstract. The Examiner has also objected to this IDS for the failure to attach a copy of the K. Dane Wittrup reference. Applicants have also attached a copy of this reference to this response.

Rejections under 35 USC § 112, second paragraph

The Examiner has rejected claim 4 under 35 USC § 112, second paragraph, as allegedly indefinite for including a reference to a phage coat protein being part of a protein translocation sequence. Applicants disagree with the Examiner's argument, but solely in the interest of expediting prosecution, have amended claim 4 to remove the reference to the protein translocation sequence. Therefore, this rejection is obviated and should be withdrawn.

The Examiner has rejected claim 9 under 35 USC § 112, second paragraph, as allegedly indefinite for the lack of antecedent basis of the claim limitation "the protein." Applicant has amended claim 9 to refer to "the first fusion protein." As such, this rejection is obviated and should be withdrawn.

Rejections under 35 USC § 102(b)

Claims 1 and 3-9 are currently pending in the application. The Examiner has rejected claims 1, 3-7 and 9 under 35 USC § 102(b) as being anticipated by Crameri (*Gene*, vol. 137, 1993, pp. 69-75). Crameri is directed to a cloning and expression

system allowing the display of cDNAs on the surface of a filamentous phage which utilizes the interaction between leucine zipper proteins. The Examiner argues that Crameri teaches a first fusion protein PIII comprising a Jun-Leucine-Zipper domain and a pelB signal sequence, as well as a second fusion protein derived from a cDNA from a cDNA library, comprising a Fos-Leucine-Zipper domain and a pelB signal sequence. The Examiner argues that a mixture of these two fusion proteins anticipates the subject matter of independent claim 1. In arriving at this conclusion, the Examiner reads the "folding state" elements out of claim 1, arguing that these limitations cannot be given patentable weight as there are no specific structures providing different folding requirements in the claims. Applicants traverse.

The claim limitations of a) iii) and b) iii) of the first and second fusion protein, respectively, of claim 1 are both defined structurally. Specifically, claim 1 requires a stretch of amino acids (i.e., both a) and b) relate to fusion proteins), whose structure provide a specific function (i.e., the ability of guiding a protein in a translocation pathway, which leads to a translocation in an unfolded (feature a) iii)) or folded (feature b) iii)) state. pelB, as disclosed in Carmeri, is a translocation sequence, which leads to translocation via a Sec-dependent pathway and, thus, leads to translocation in an unfolded state. Hence, the first fusion protein in Crameri leads to translocation in an unfolded state. However, the second fusion protein in Crameri also comprises a pelB sequence and, thus, a translocation sequence which does not provide for translocation in a folded state. Accordingly, the second fusion protein does not comprise a translocation domain having the structural and functional features of feature b) iii). One preferred example of such a sequence is the Tat-dependent translocation sequence.

Therefore, even assuming arguendo that Crameri discloses the first fusion protein of present claim 1, it does not disclose the second fusion protein of present claim 1. As such, the anticipation rejection of claim 1, and its dependent claims, is improper and should be withdrawn.

Rejections under 35 USC § 103(a)

The Examiner has rejected claims 1 and 3-9 under 35 USC § 103(a) as being obvious over Crameri (*Gene*, vol. 137, 1993, pp. 69-75) in view of Weiner (US Pat. No. 6,335,178) and further in view of Wu (*Arch. Microbiol.*, vol. 173, 2000, pp. 319-324). Crameri is discussed above. Weiner is directed to compositions and methods for secretion of functional proteins in a soluble form in host cells. Wu is directed to the membrane targeting and translocation of periplasmic and membrane-bound bacterial hydrogenases. The Examiner has also rejected claims 1 and 3-9 under 35 USC § 103(a) as being obvious over Crameri (*Gene*, vol. 137, 1993, pp. 69-75) in view of Georgiou (US Pat. No. 7,419,783). Crameri is discussed above. Georgiou is directed to leader peptides which direct export of heterologous proteins from the bacterial cytoplasm.

The Examiner argues that Crameri is the closest prior art to the subject matter Jun-Leucine-Zipper domain and a Fos-Leucine-Zipper domain, respectively, and a pelB signal sequence, which leads to the transport in an unfolded state into the periplasm. Further, the Examiner argues that Weiner in view of Wu, or Georgiou teach such a translocation sequence by disclosing a Tat-dependent translocation sequence which allegedly motivates the skilled person to modify the protein mixture of Crameri by

introducing a Tat-dependent signal sequence in one of the fusion proteins. Hence, the subject matter of claim 1 is considered obvious. Applicants traverse.

The deficiencies of Crameri are discussed above. None of Weiner, Wu or Georgiou compensate for these deficiencies. Furthermore, one of skill in the art would not combine Crameri with Weiner and Wu, or Crameri with Goergiou. To arrive at the subject matter of present independent claim 1, one of skill in the art would have to recognize the possibility of at least modifying a protein mixture like the one of Crameri in a way that one of the fusion proteins is folded in the cytoplasm and is subsequently transported into the periplasm, where it can bind to another fusion protein which has been folded in the periplasm. That is, one of skill in the art would have to consider how to produce protein complexes containing fusion proteins of which some are folded in the periplasm and others in the cytoplasm. However, Crameri neither teaches nor suggests that its proteins can be modified in such a manner. To the contrary, Crameri states on page 74, right column, 2nd paragraph: "the potential for the expression of dimers is mainly limited by the imagination of the investigator", which suggests to the skilled person that the system of Crameri allows for the production of any desired fusion protein. This then teaches one of skill in the art away from using any other method of producing fusion proteins. In addition, none of Weiner, Wu or Georgiou teach or suggest modifying the Crameri proteins in such a manner. Hence, there is no motivation whatsoever for the skilled person to modify the protein mixture taught in Crameri at all, let alone to modify it by introducing features taught in Weiner, Wu, or Georgiou.

Furthermore, a skilled person would not have expected that two proteins, one of which has been folded in the cytoplasm, the other one transported unfolded into the

periplasm could have been capable of interacting in the periplasm to form fusion protein dimers capable of presenting. Hence, there was no reasonable expectation of success and no motivation to try the claimed approach, which is why the subject matter of present claim 1 is not obvious over Crameri in view of Weiner and Wu, or in view of Georgiou. Therefore, this obviousness rejection is improper and should be withdrawn.

In view of the foregoing, it is submitted that the present application is now in condition for allowance. Reconsideration and allowance of the pending claims are requested. The Director is authorized to charge any fees or credit any overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

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